UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM:

To: BeWanda Alexander

From: Clayton Myers, Entomologist **Date**: March 14, 2012

3-14-12

Subject: PRODUCT PERFORMANCE DATA EVALUATION RECORD

DP barcode:	385561, 385623, 393362
Decision no.:	440307
Submission no:	882827, 902307
Action code:	R110.0
Product Name:	PNR 1427 Insecticide
EPA Reg. No or File Symbol:	11556-RLL
Formulation Type:	RTU Pet Collar

Ingredients statement from the label with PC codes included: Flumethrin, 4.50% PC: 36007; Imidacloprid, 10.00%, PC: 129099

Application rate(s) of product and each active ingredient (lbs. or gallons/1000 square feet or per acre as appropriate; and g/m^2 or mg/cm^2 as appropriate): One collar per animal, cut to fit with some slack around neck (varies somewhat upon animal size). Claims through 8 months for some pests, including waterproof/washing/water immersion.

I. Action Requested: Data was submitted to support pest claims for a ready to use, indoor, non-food product; a companion animal collar impregnated with 2 active ingredients.

II. Background: The registrant seeks to register a flumethrin/imidacloprid combo pet collar product for control of fleas and ticks and lice on dogs, and fleas and ticks on cats. The registrant has submitted 20 studies to support efficacy claims.

III. MRID Summaries: (Primary Review attached)

a. MRID 48576501

(1) GLP study

(2) A laboratory study was conducted to evaluate killing efficacy of the test product against Deer ticks, *Ixodes scapularis* adults and nymphs against hair taken from treated animals via an *in vitro* exposure study. Three dogs were acclimated and used for this study, with 2 animals provisioned with the treated collars (one as a backup), and one left as an untreated control. Pre-treatment hair samples were taken and tick exposures conducted to confirm no insecticidal activity of untreated hair. Periodically after treatment, through 240 days (8 months), hair samples were taken from the test dog and control dog from various body surfaces. One gram of hair was placed into each of 6 Petri dishes to which were added 10 nymph and 10 adult ticks. Counts of live and dead ticks were made after 48 hours of exposure. Mortality was calculated using Abbott's formula.

(3) Efficacy for all exposures and all tick stages exceeded 97% through 240 days after initial placement of the collar, with most of the exposures resulting in 100% control. Authors conclude

that efficacy is supported for Deer ticks. The primary reviewer concurred that the data was adequate to support 8 month efficacy claims Deer ticks, but noted that the collars were not exposed to any weathering and thus the claims were only supportive of dogs kept indoors.
(4) The study is acceptable to 8 month control claims against Deer ticks, *Ixodes scapularis*, on dogs, with control starting within 48 hours of collar placement.

b. MRID 48576502

(1) GLP study
(2) A laboratory study was conducted to evaluate killing efficacy of the test product against Deer ticks, *Ixodes scapularis* adults on dogs treated with the collar. Dogs were acclimated and pre-qualified for tick retention. 16 dogs were used in the study with 8 each (4 males and 4 females) allocated to either a treatment or control group. 50 ticks were placed on each dog one day prior to placement of collars. Dogs under 18 lbs received a small collar and larger dogs received the large collar. Ticks were counted 2 days after placement of collars via removal. Periodic re-infestations were made onto the dogs, with counts and removal at 48 hours. The study was carried through 247 days (8 months). Mortality was calculated using Abbott's formula.
(3) Efficacy for all exposures and all tick stages exceeded 96% through 247 days after initial placement of the collar, with most of the exposures resulting in 100% control. Authors conclude that efficacy is supported for Deer ticks. The primary reviewer concurred that the data was adequate to support 8 month efficacy claims Deer ticks, but noted that the collars were not exposed to any weathering and thus the claims were only supportive of dogs kept indoors.
(4) The study is acceptable to 8 month control claims against Deer ticks, *Ixodes scapularis*, with control starting within 48 hours of collar placement.

c. MRID 48240116

(1) GLP study
(2) A laboratory study was conducted to evaluate killing efficacy of the test product against *Dermacentor variabilis* and *Rhipicephalus sanguineus* ticks and *Ctenocephalides felis* fleas on dogs treated with the collar. Dogs were acclimated and pre-qualified for flea retention. 16 dogs were used in the study with 8 each (4 males and 4 females) allocated to either a treatment or control group. 50 ticks of each species and 100 fleas were placed on each dog one day prior to placement of collars. All dogs were over 18 lbs. and thus, all dogs received the large collar. Ticks and fleas were counted 2 days after placement of collars via removal. Periodic re-infestations were made onto the dogs, with counts and removal at 48 hours. The study was carried through 254 days (8 months). Mortality was calculated using Abbott's formula.
(3) Flea efficacy for all exposures exceeded 96% through 246 days after initial placement of the collar. Flea efficacy upon the day 7 re-infestation was also greater than 90% within 2 hours of re-infestation. Tick efficacy for both species exceeded 90% through 240 days after initial placement, except for the 2 day assessment, which was inadequate (likely due to the time taken for the material to spread through the dogs hair initially). Authors conclude that efficacy is supported for fleas and ticks. The primary reviewer concurred that the data was adequate to support 8 month efficacy claims for American Dog Ticks, Brown Dog Ticks, and Fleas, but noted that the collars were not exposed to any weathering and thus the claims were only supportive of dogs kept indoors.
(4) The study is acceptable to 8 month control claims against Ticks (ABT and BDT) and fleas, with control starting within 48 hours of collar placement for fleas.

d. MRID 48240117

(1) GLP study
(2) A laboratory study was conducted to evaluate killing efficacy of the test product against *Amblyomma americanum* adult ticks and *Ctenocephalides felis* fleas on cats treated with the collar. Cats were acclimated and pre-qualified for flea retention. 16 domestic short-hair cats were used in the study with 8 each (mixed sex) allocated to either a treatment or control group. 50 ticks and 100 fleas were placed on each cat one day prior to placement of collars. Ticks and fleas were

counted 2 days after placement of collars via removal. Periodic re-infestations were made onto the cats, (alternating between fleas and ticks over the course of the study) with counts and removal at 48 hours. The study was carried through 246 days (8 months). Mortality was calculated using Abbott's formula.
(3) Flea efficacy for all exposures exceeded 90% through 246 days after initial placement of the collar (8 months). Flea efficacy upon the day 7 re-infestation was also greater than 90% within 2 hours of re-infestation. Tick efficacy exceeded 90% through 240 days after initial placement, except for the 2 day assessment, which was inadequate (likely due to the time taken for the material to spread through the cats' hair initially). Authors conclude that efficacy is supported for fleas and ticks. The primary reviewer concurred that the data was adequate to support 8 month efficacy claims for Lone Star Ticks, and Fleas, but noted that the collars were not exposed to any weathering and thus the claims were only supportive of cats kept indoors.
(4) The study is acceptable to 8 month control claims against *Amblyomma americanum* and fleas on cats, with control starting within 48 hours of collar placement for fleas.

e. MRID 48240118

(1) GLP study
(2) A laboratory study was conducted to evaluate killing efficacy of the test product against *R. sanguineus* and *D. variabilis* adult ticks and *Ctenocephalides felis* fleas on dogs treated with the collar after water immersion and shampooing. Dogs were acclimated and pre-qualified for flea retention. 32 dogs were used in the study with 8 each allocated to 4 groups: Treated immersed, Treated shampooed, Untreated immersed, Untreated shampooed. Shampooing was conducted monthly and the immersion group was immersed in water monthly. 50 ticks of each species and 100 fleas were placed on each dog at times prior to placement of collars. Ticks and fleas were counted 2 days after placement of collars via removal. Periodic re-infestations were made onto the dogs, with counts and removal at 48 hours. The study was carried through 232 days (7 months). Mortality was calculated using Abbott's formula.
(3) Flea efficacy for the shampoo group exceeded 90% through day 225. For water immersion, efficacy only exceeded 90% though day 141. *R. sanguineus* efficacy exceeded 90% though day 232 for both groups. *D. variabilis* efficacy exceeded 90% though day 225 for shampooing but only day 197 for water immersion. The primary reviewer concurred with the author's conclusion that data was adequate to support 8 month claims for prevention of fleas and ticks when shampooed once per month. Because *D. variabilis* efficacy was only adequate for 7 months and flea efficacy was only adequate through day 141, only a 5 month claim would be acceptably supported. The reviewer also states that the label must specify that bathing/swimming should be no more than once per month for the claims to be supported by this data set.
(4) The study is acceptable to support 8 month claims against fleas and ticks for dogs that are shampooed no more than once per month. For dogs that swim once per month, flea claims are limited to 5 months and tick claims to 7 months.

f. MRID 48240119

(1) GLP study
(2) A laboratory study was conducted to evaluate killing efficacy of the test product against *Ixodes ricinus* adult ticks and *Ctenocephalides felis* fleas on cats treated with the collar. Cats were acclimated and pre-qualified for flea retention. 20 domestic short-hair cats were used in the study with 10 each (mixed sex) allocated to either a treatment or control group. 40 ticks were placed on each cat two days prior to placement of collars. 100 fleas were placed on the day before treatment. Ticks and fleas were counted 2 days after placement of collars via removal. Periodic re-infestations were made onto the cats, (alternating between fleas and ticks over the course of the study) with counts and removal at 48 hours. The study was carried through 237 days (8 months). Mortality was calculated using Abbott's formula.
(3) Tick efficacy for all exposures exceeded 90% through 239 days after initial placement of the collar (8 months), except for the 2 day assessment, which was inadequate (likely due to the time taken for the material to spread through the cats' hair initially). Flea efficacy exceeded 90%

through 239 days after initial placement. Authors conclude that efficacy is supported for fleas and ticks. The primary reviewer concurred that the data was adequate to support 8 month efficacy claims for Ticks, and Fleas.
(4) Because *Ixodes ricinus* is a species known to have similar susceptibility to *Ixodes scapularis* the data are adequate to support 8 month efficacy claims for *Ixodes* ticks. For fleas, the study is acceptable to 8 month control claims on cats.

g. MRID 48240120

(1) GLP study
(2) A laboratory study was conducted to evaluate killing efficacy of the test product against *Ixodes ricinus* and *Rhipicephalus sanguineus* ticks and *Ctenocephalides felis* fleas on dogs treated with the collar. Dogs were acclimated and pre-qualified for flea retention. 20 dogs were used in the study with 10 each allocated to either a treatment or control group. 40-50 ticks of each species and 100 fleas were placed on each dog two days prior to placement of collars. All dogs were over 18 lbs. and thus, all dogs received the large collar. Ticks and fleas were counted 2 days after placement of collars via removal. Periodic re-infestations were made onto the dogs, with counts and removal at 48 hours. The study was carried through 237 days (8 months). For female ticks, engorgement was determined for female ticks. Mortality was calculated using Abbott's formula. To evaluate repellency, ticks attached to the dogs on day -8 (pre-qualifying) were counted at 3 and 6 hours after placement to verify the appropriateness of time points for evaluation. Tick counts for repellency determination was done the same way after every re-infestation without removal of ticks. A flea larvicidal assessment was conducted on days -7 to -5, and then in 2 to 5 week intervals from day 12 forward to when dogs were not infested with parasites. Fleece-lined board were placed on the floors of dog kennels for 3 hours on 3 consecutive days. Samples were cut from the blankets, placed in petri dishes, and frozen. Remaining parts of the blanket were also frozen and stored. The wooden board was cleaned and a new blanket fixed. After removal from the freezer, petri dishes were allowed to reach room temperature and ~50 flea eggs from the same colony were placed in the middle of the blanket sample. Flea rearing medium was spread over the surface and samples were incubated for 28 days.
(3) Tick efficacy for both species exceeded 90% through 238 days after initial placement, except for the 2 day assessment, which was inadequate (likely due to the time taken for the material to spread through the dogs hair initially). Tick repellency, within hours of placement, for both species exceeded 90% from 27 to 236 days after initial treatment. Adult flea efficacy exceeded 99% from day 2 to day 238 after treatment. Larvicidal effects against fleas exceeded 99% for days 12-245 after treatment. The primary reviewer concurred that the study was adequate to support 8 month flea and tick claims.
(4) Because *Ixodes ricinus* is a species known to have similar susceptibility to *Ixodes scapularis* the data are adequate to support 8 month efficacy claims for *Ixodes* ticks. For *R. sanguineus* and fleas, the study is acceptable to 8 month control claims against ticks and fleas.

h. MRID 48240121

(1) non-GLP study
(2) A laboratory study was conducted to evaluate killing efficacy of the test product against *Ixodes ricinus* adult ticks and *Ctenocephalides felis* fleas on cats treated with the collar. Cats were acclimated and pre-qualified for flea retention. 20 domestic short-hair cats were used in the study with 10 each (mixed sex) allocated to either a treatment or control group. 40 ticks were placed on each cat two days prior to placement of collars. 100 fleas were placed on the day before treatment. Ticks and fleas were counted 2 days after placement of collars via removal. Periodic re-infestations were made onto the cats, (alternating between fleas and ticks over the course of the study) with counts and removal at 48 hours. The study was carried through 237 days (8 months). Mortality was calculated using Abbott's formula. To evaluate repellency, ticks attached to the cats on day -8 (pre-qualifying) were counted at 3 and 6 hours after placement to verify the appropriateness of time points for evaluation. Tick counts for repellency determination was done the same way after every re-infestation without removal of ticks. A flea larvicidal assessment was

conducted on days -7 to -5, and then in 2 to 5 week intervals from day 12 forward to when cats were not infested with parasites. Fleece-lined board were placed on the floors of cat transport boxes for 3 hours on 3 consecutive days. Samples were cut from the blankets, placed in petri dishes, and frozen. Remaining parts of the blanket were also frozen and stored. The wooden board was cleaned and a new blanket fixed. After removal from the freezer, petri dishes were allowed to reach room temperature and ~50 flea eggs from the same colony were placed in the middle of the blanket sample. Flea rearing medium was spread over the surface and samples were incubated for 28 days. Efficacy against flea eggs was evaluated by rearing flea eggs with debris that fell out of the cats' hair (100 mg of debris : 100 mg of flea medium). Eggs were incubated for 4 days and hatch was evaluated.

(3) Tick efficacy for all exposures exceeded 90% through 239 days after initial placement of the collar (8 months), for both killing and repellence (237 days). Flea efficacy exceeded 90% through 169 days after initial placement. Larvicidal efficacy exceeded 90% through 37 days. Ovicidal efficacy never reached 90% for flea eggs. Authors conclude that efficacy is supported for fleas and ticks. The primary reviewer concurred that the data was adequate to support 8 month efficacy claims for Ticks. For fleas, the supported efficacy duration was shorter. The author concurred that use of the collar could aid in the control of flea larvae, and thus other fleas in the pets environment.

(4) Because *Ixodes ricinus* is a species known to have similar susceptibility to *Ixodes scapularis* the data are adequate to support 8 month efficacy claims for *Ixodes* ticks. For fleas, the study is acceptable to support a 5 month claim on flea adults, and an aids in control claim for flea larvae. No larvicidal claims are supported.

i. MRID 48240122

(1) non-GLP study

(2) A clinical field study was conducted using parasite infested animals. The study enrolled 346 animals from France, Germany, Hungary, and Portugal.

(3) The study is rated supplemental regarding claims on the label for pests found in the United States.

j. MRID 48240123

(1) non-GLP study

(2) A clinical field study was conducted using parasite infested animals. The study enrolled 346 animals from France, Germany, Hungary, and Portugal.

(3) The study is rated supplemental regarding claims on the label for pests found in the United States.

k. MRID 48240124

(1) non-GLP study

(2) A laboratory study was conducted to evaluate the onset of efficacy against cat fleas, *Ctenocephalides felis* on cats. Cats were acclimated and pre-qualified for flea retention. 16 domestic short-hair cats were used in the study with 8 each (mixed sex) allocated to either a treatment or control group. After qualification, 100 fleas were placed on each cat on the day of placement of collars. Fleas were counted 1 day after placement of collars via removal. Mortality was calculated using Abbott's formula.

(3) Flea efficacy at one day after placement (and treatment) was 99.8%. The study authors indicate the study is acceptable to support a claim that the product controls fleas within 24 hours. The primary reviewer concurs with this conclusion.

(4) The study is acceptable to support claims against fleas on cats for killing within 24 hours.

l. MRID 48240125

(1) non-GLP study

(2) A laboratory study was conducted to evaluate the onset of efficacy against cat fleas, *Ctenocephalides felis* on dogs. Dogs were acclimated and pre-qualified for flea retention. 16 dogs

were used in the study with 8 each (mixed sex) allocated to either a treatment or control group. After qualification, 100 fleas were placed on each cat on the day of placement of collars. Fleas were counted 1 day after placement of collars via removal. Mortality was calculated using Abbott's formula.
(3) Flea efficacy at one day after placement (and treatment) was 100.0%. The study authors indicate the study is acceptable to support a claim that the product controls fleas within 24 hours. The primary reviewer concurs with this conclusion.
(4) The study is acceptable to support claims against fleas on dogs for killing within 24 hours.

m. MRID 48240126

(1) non-GLP study
(2) A laboratory study was conducted to evaluate the killing efficacy of flumethrin against 2 *Ixodes* species in an in vitro exposure assay. Flumethrin was dissolved in acetone and transferred into snap cap vials and centrifuged for 2 hours at room temperature. Vials were uncapped and acetone was evaported to leave a uniform coating on the inside of the vial (44.7 sq cm). Five unfed ticks were transferred to each vial, capped, and kept at room temperature. Efficacy was evaluated by placing vials to a heating table to observe ticks for heat avoidance behavior, after 24 and 48 h exposure. There were 7 dosages tested along with untreated and solvent control groups. There were 6 reps per concentration per tick species, with 5 ticks per vial. Inferential statistical analysis was performed using repeated measures ANOVA with concentration, tick species, and time as fixed effects in the model. The 2 and 3 way interactions were also included as mixed effects into the model.
(3) 24 hour tick efficacy for all species exceeded 90% at doses of 0.288 ppm and higher. For 48 hours, >90% efficacy was observed at doests of 0.0576 ppm and higher. Study authors say these data suggest similar susceptibility responses of the 2 *Ixodes* spp. toward flumethrin.
(4) The study is rated as supplemental, as the data are based upon technical grade active ingredient, and other product specific collar data have already been submitted to support tick efficacy claims. However, the data are acceptable to demonstrate that efficacy data between the two *Ixodes* species are similar and could be used to support bridging arguments for *Ixodes* efficacy data between the two species.

n. MRID 48240127

(1) non-GLP study
(2) A laboratory study was conducted to evaluate the onset of activity of the submitted collar against *Ixodes ricinus* on cats. 16 cats were assigned to either a treated or control group (8 cats per group). Cats were prequalified for tick retention. Cats were infested with 20 adult female and 15 adult male ticks on SD -6, 0, and 2 (cats were sedated). On SD 2, female ticks were counted and removed at 48 hours after treatment. After re-infestation, tick counts for repellency were made at 6 h after re-infestation. After tick removal, engorgement status was determined. For determination of repellency, the female ticks were specified during counting as dead or alive. Efficacy (mortality or repellency) was calculated using Abbott's formula, and compared statistically between the 2 groups using a 2 tailed Wilcoxon-Mann-Whitney-U-test ($p = 0.05$).
(3) Killing efficacy for ticks at 48 hours after treatment was 95.5%. Repelling efficacy at 6 hours after the SD 2 re-infestation was 100%.
(4) The study is acceptable to support killing claims against *Ixodes* ticks on cats within 48 hours and supports the claims of preventing tick infestations within 48 hours after initial application on cats.

o. MRID 48240128

(1) non-GLP study
(2) A laboratory study was conducted to evaluate efficacy against *Ixodes ricinus* ticks on dogs. 14 dogs (7 per treatment) were used in the study, and were housed in individual pens with petroleum jelly barriers to prevent escape of ticks. On SD -2, 40 ticks were placed on each dog. On SD 0, the dogs assigned to the collar group were fitted. Reinfestations were made on days 7, 28, 56, 84,

112, 133, 168, 196, 223, and 238 with 35 ticks placed on each dog. Ticks were counted at 48 h after each infestation. On SD 0, live attached ticks were counted without removal. Efficacy was calculated using Abbott's Formula.
(3) Killing control efficacy for day 2 wasy 89.9, and was 100% for all other reinfestations through day 240.
(4) The study is acceptable to support claims against *Ixodes ricinus* for 8 months.

p. MRID 48240129

(1) non-GLP study
(2) A laboratory study was conducted to evaluate the onset of activity of the submitted collar against *Ixodes ricinus* and *Rhipicephalus sanguineus* on dogs. 16 dogs were assigned to either a treated or control group (8 dogs per group). Dogs were prequalified for tick retention. Dogs were infested with 20 adult female and 15 adult male *Ixodes* ticks and 50 mixed sex *Rhipicephalus* ticks on SD -5, 0, and 2 (cats were sedated). On SD 2, female *Ixodes* ticks and all *Rhipicephalus* were counted and removed at 48 hours after treatment. After re-infestation, tick counts for repellency were made at 6 h after re-infestation. After tick removal, engorgement status was determined. For determination of repellency, the female ticks were specified during counting as dead or alive. Efficacy (mortality or repellency) was calculated using Abbott's formula, and compared statistically between the 2 groups using a 2 tailed Wilcoxon-Mann-Whitney-U-test ($p = 0.05$).
(3) Killing efficacy for ticks at 48 hours after treatment was 96.8% for *R. sanguineus* and 96.2% for *Ixodes*. Repelling efficacy at 6 hours after the SD 2 re-infestation was 99.2% for *R. sanguineus* and 100% for *Ixodes*.
(4) The study is acceptable to support killing claims against *Ixodes* and *R. sanguineus* ticks on dogs within 48 hours and supports the claims of preventing tick infestations within 48 hours after initial application on dogs.

q. MRID 48240130

(1) non-GLP study
(2) A laboratory study was conducted to evaluate the killing efficacy of flumethrin/imidacloprid against 3 tick species (*Ixodes ricinus*, *Rhipicephalus sanguineus*, and *Dermacentor reticulatus*) in an in vitro exposure assay. An appropriate amount of the test compound mixture (1:1.85 flumethrin: imidacloprid) was dissolved in acetone and transferred into snap cap vials and centrifuged for 2 hours at room temperature. Vials were uncapped and acetone was evaported to leave a uniform coating on the inside of the vial (44.7 sq cm). Five unfed adult ticks, 10 unfed nymphs, or approximately 25 unfed larvae were transferred to each vial, capped, and kept at room temperature. Efficacy was evaluated by placing vials to a heating table to observe ticks for heat avoidance behavior, after 24 and 48 h exposure. There were 8 dosages tested along with untreated and solvent control groups. There was one repolicate per treatment per tick species. Inferential statistical analysis was performed using repeated measures ANOVA with concentration, tick species, and time as fixed effects in the model. The 2 and 3 way interactions were also included as mixed effects into the model.
(3) 24 and 48 hour efficacy for all stages of *Ixodes ricinus* ticks was >90% for concentrations of 7.2 ppm and higher of test material. 24 and 48 hour efficacy for all stages of *Rhipicephales sanguineus* was >90% for concentrations of 1.44 ppm and higher. 24 and 48 hour efficacy for all stages of *Dermacentor reticulatus* ticks was >90% for concentrations of 0.288 ppm and higher.
(4) The study is rated as supplemental, as the data are based upon technical grade active ingredients, and other product specific collar data have already been submitted to support tick efficacy claims.

r. MRID 48240131

(1) non-GLP study
(2) A laboratory study was conducted to evaluate the killing efficacy of a pet collar against existing natural infestations of dog lice, *Trichodectes canis*. 18 dogs were evaluated in the study, with 9 dogs placed in either a control or treated group. Natural lice infestations were evaluated by

counts at 8 specified sites on each dog and lice were not removed. On SD's -5, -2, -1, 2, 7, 14, 21, 28, and 35, lice counts were made for each dog for a minimum of 5 minutes per dog. Counts at a number of sites were determined based upon finding lice at sites specified in the study. Effectiveness was calculated using Abbott's formula, based upon pre and post-treatment counts for each dog at each interval. Infestation was defined as a dog having at least one louse and viable eggs present or >/= 10 live lice. The effectiveness threshold was set at 95%. Lice counts were also compared statistically using ANOVA.
(3) 48 hour efficacy was 95.1% and efficacy was 100% for the remainder of the study.
(4) The study is acceptable to support claims against dog lice (*Trichodectes canis*) for one month on dogs. Claims longer than one month are not supported by this data set.

s. MRID 48240132

(1) GLP study
(2) A laboratory study was conducted to evaluate the killing efficacy of a pet collar against existing natural infestations of sarcoptic mange mites, *Sarcoptes scabiei*. 10 dogs were evaluated in the study, and were determined to be infested with *S. scabiei* but not *Demodex spp.* There was no control group. Dogs were subject to mite counts via skin scrapings on days -2, 29, 60, and 90 from 5 different body areas suspected of being infested. Scrapes were made with a blade to that capillary oozing occurred. The scraping was transferred to a marked microscope slide containing mineral oil for examination for the presence of live mites. Clinical signs and extent of scabietic lesions on each dog were assessed on the days when scrapings were made, and classified via a qualitative scale for scales, and hair loss. Photographs were taken to assist in these qualitative assessments. An overall success rate was calculated by dividing the number of dogs with no live mites by the total number of dogs in the group and multiplying by 100. The study authors defined effectiveness as a success rate that was >/= 90%.
(3) Mite presence was reduced to 10% on days 29 and 60, with 0% mite occurrence by day 90. The percent of dogs showing papules on skin decreased from 75% to 20% by day 90, and skin crusting was reduced similarly. Study authors conclude that since mite numbers were reduced by 100% over the course of the study (along with the other clinical measurements), that the study should support claims against sarcoptic mange mites.
(4) The primary reviewer points out that the lack of a control group is a deficiency, but that overall evidence of mite reduction is acceptable given the design of the study. The study is partially acceptable, and can be used to support an "aids in control" or "aids in treatment" claim for Sarcoptic mange.

t. MRID 48240133

(1) non-GLP study
(2) An *in vitro* laboratory study was conducted to evaluate the killing efficacy (speed of kill) for hair clipped from animals treated with a a pet collar--against brown dog tick, *Rhipicephalus sanguineus.* 2 predecessor studies were conducted where hair was clipped from treated animals from various parts of the animal's bodies. For this study, a chest hair sample was taken with a flumethrin content that was most equivalent to the mean group was chosen for a contact test to evaluate the onset of efficacy. Approximately 0.1g of each sample of the left and right chest were taken, weighed, and mixed; for both cats and dogs. 6 unfed adult ticks were counted into glass vials on SD -3 and kept in an incubator. On SD 0, the ticks were placed onto treated hair samples in petri dishes and kept in an incubator. Tick status was evaluated at 2, 6, 8, 12, 24, and 48 h after initial contact. The study was repeated at 7, 14, 21, 30, 59, 90, 120, 149, 181, 210, and 240 days after initial animal treatment with the collar. Status was assessed by visual examination of the ticks reaction to a heating plate. Mortality was assessed and %Efficacy was calculated using Abbott's formula.
(3) For dogs, all ticks were alive at the 2 h examination for every treatment duration. Efficacy reached 100% by the 6 hour examination for all treatment intervals through 210 days. At 240 days, the efficacy did not exceed 90% until 12 hours of exposure had elapsed, but 83% efficacy was observed from 6-8h. For cats, all ticks were alive at the 2 h examination for every treatment

duration. Efficacy reached 100% by the 6 hour examination for all treatment intervals through 210 days. At 240 days, the efficacy did not exceed 90% until 8 hours of exposure had elapsed, but 50% efficacy was observed at 6h. The study author argues that taking atactic ticks would not be able to attach to skin, overall efficacy in dog and cat hair exceeds 98% after 6 h exposure.
(4) The primary reviewer points out that the lack of a control group is a deficiency, as efficacy was based upon comparisons with SD -1 data. The data supports the addition of *R. sanguineus* claims for dogs within 6 hours after initial efficacy has been obtained, and re-infesting ticks are controlled as quickly as 6 hours. Claims against ticks are supported for cats, but not for the 6 hour onset of activity.

u. MRID 48240134

This study contains data in support of an imidacloprid spot-on product that is not applicable to this submission. It is rated as supplemental.

v. MRID 48240137

This study contains data in support of an imidacloprid spot-on product that is not applicable to this submission. It is rated as supplemental.

IV. RECOMMENDATIONS:

(1) Labeling:

(a) What pests and site/pest combinations may be added as follows to the label based on the submitted or cited data?

For 8 month prevention and treatment of ticks, fleas, on dogs and cats.
For 1 month prevention and treatment of lice on dogs
Kills ticks within 48 hours of treatment or re-infestation
Kills fleas within 24 hours of treatment or re-infestation
Aids in control of flea larvae in pet's environment
Kills lice on dogs
Kills ticks within 6 hours of reinfestation on dogs
Kills re-infesting fleas (after initial 7 days) within 2 hours

(b) What pests and site/pest combinations must be removed from the label?

Claims against lice must not exceed 1 month
Waterproof claims must be clarified as followed:
-In order to maintain an 8 month control duration, dogs must not be bathed more than once per month
-If dogs swim once per month, the control duration must be revised to 5 months
-Water exposure (i.e. immersion, bathing, or prolonged exposure to rain) can only be once per month
Tick claims for killing within 6 hours of reinfestation on cats must be removed—the claim only is supported for dogs.

(c) List changes to the directions for use:

Remove the directions for killing roaches and ants ('in the environment') on page 2.

(d) List changes to the optional marketing claims:

Claims against lice must be limited to one month
All claims related to '8 months' must be limited to fleas and ticks only. Other pests are not controlled for that

duration.

All claims related to control of flea larvae in the pet's environment must be removed or revised to 'aids on control' for fleas in the pet's environment. This product does not provide efficacy as an area-wide/premise treatment against flea larvae.

All disease claims must be deleted, unless the claim is stated "kills/controls xxx pest that may vector yyy."

All claims of "breaking the flea life cycle" must be deleted. This claim implies efficacy against flea eggs and larvae similar to IGR products that are specifically designed to break the flea life cycle for months. This product does not have that level of efficacy against eggs and larvae.